Chapter 104

Physiologic and Pathologic Responses to Heat Stress

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Temperatures low enough to freeze tissue, and temperatures higher than about 45°C (113°F) (1), can directly injure living tissue. Even within these limits, temperature changes alter biological function both through configurational changes that affect the function of protein molecules, such as enzymes, receptors, and membrane channels, and through a general effect on chemical reaction rates. Most reaction rates vary approximately as an exponential function of temperature within the physiologic range, and raising temperature by 10°C increases the reaction rate two- to threefold. A familiar clinical example of the effect of body temperature on metabolic processes is the rule that each 1°C of fever increases a patient's fluid and calorie needs 13% (2). Homeotherms, through their thermoregulatory processes, keep their internal or body *core* temperatures within a fairly narrow range near 37°C (98.6°F), and thus provide a more stable physicochemical environment for their biological processes. (Temperatures of the skin and superficial tissues, of course, vary more widely.)

The level of normal body temperature is conventionally given as 37°C (98.6°F), and this figure may create a misleading impression of the constancy of body temperature. Core temperature at rest undergoes a daily or circadian rhythm, with an amplitude of about 1°C, and is lowest in the early morning and highest in the late afternoon (3–5). In women of childbearing age, this circadian rhythm is superimposed on another rhythm, with a somewhat smaller amplitude, associated with the menstrual cycle (6–8). These rhythms are produced by underlying rhythms in the control of the thermoregulatory responses, in what we may think of as the setting of the body's "thermostat." These rhythms, plus other factors such as individual variation and acclimatization to heat, account for a range of core temperatures of healthy subjects at rest (Figure 104-1). In addition core temperature may increase several degrees with heavy exercise or fever; still higher temperatures may result from extreme conditions of exercise, neurologic disease, or heat stress that overwhelm the capacity of the thermoregulatory system.

Adverse effects of heat stress include impairment of physical and mental performance (9,10), heat-related illnesses and syndromes (11–13), aggravation of other preexisting illnesses, and direct injury caused by high tissue temperatures. Direct thermal injury includes burns (which, however, are not the subject of this chapter) and perhaps some injury associated with heat stroke. In healthy people, however, the thermoregulatory responses are ordinarily so powerful and effective that tissue temperatures rarely reach harmful levels during heat stress, and most adverse effects of heat stress owe much more to secondary consequences of thermoregulatory and other homeostatic responses than they do to direct thermal injury to tissue. This chapter discusses normal physiologic responses to heat and to combined exercise-heat stress, events that lead to deterioration of performance in the heat or frank heat illness, factors that affect heat tolerance and susceptibility to heat-related illnesses, and preventive measures. In addition, clinical aspects of heat illness are briefly summarized.

REGULATION OF BODY TEMPERATURE

Physiologic and Behavioral Temperature Regulation

Two distinct control systems, physiologic and behavioral, operate in parallel to regulate body temperature. Physiologic

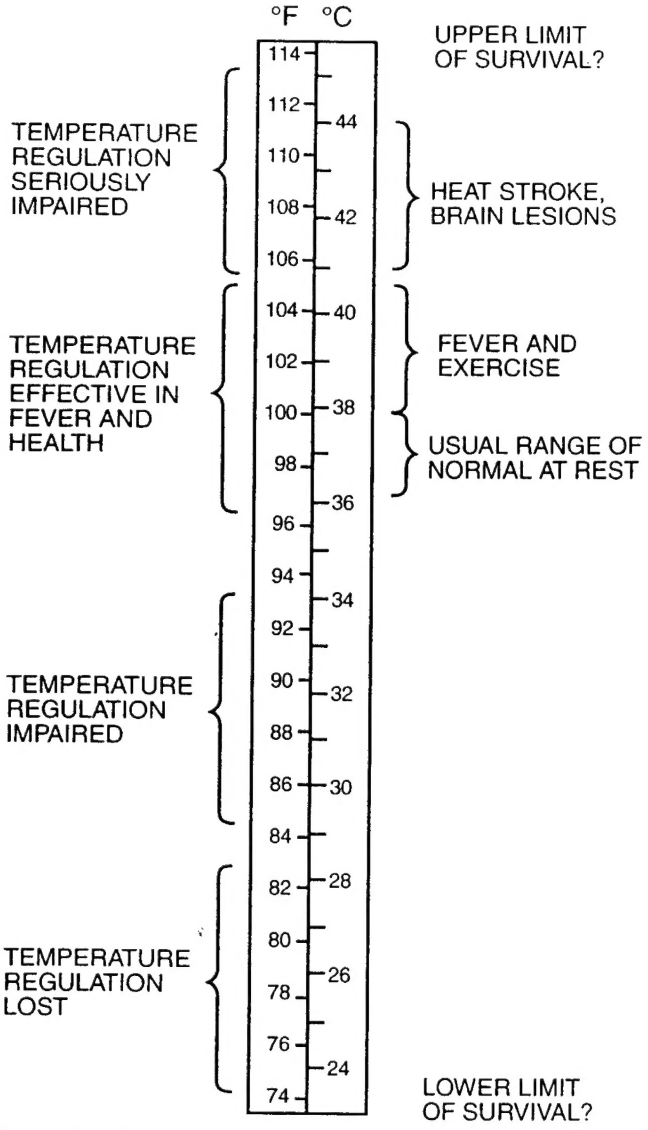

Figure 104-1 Ranges of rectal temperature found in healthy persons, patients with fever, and in persons with impairment or failure of thermoregulation. (Modified with permission of the publisher from DuBois EF. Fever and the regulation of body temperature. Spring field IL: Charles C Thomas, 1948.)

thermoregulation employs involuntary responses. In humans the most important physiologic responses for thermoregulation in the heat are 1) vasomotor responses, which control blood flow from the interior of the body to the skin, and 2) sweating. (In addition, hyperthermic humans often pant, but panting is not a major avenue of heat loss in humans.) The physiologic control system is capable of fine adjustments in these responses, and enables homeotherms to achieve fairly precise regulation of their core temperatures. These responses will be discussed further below. Behavioral thermoregulation involves the conscious, willed use of whatever means are available, and operates primarily to reduce the level of thermal discomfort. Since thermal discomfort is closely related to the underlying physiologic strain (14), behavioral thermoregulation reduces the demand on the physiologic thermoregulatory responses. Familiar behavioral responses to heat stress include shedding excess clothing, reducing physical activity to decrease heat production, seeking a more comfortable environment, and drinking cool fluids. Behavioral thermoregulation is strongly influenced by learned responses, and may be compromised or overridden when there is enough motivation to persist in a situation that produces a high degree of thermal stress, as during intense physical training or athletic competition, or in the performance of certain jobs. In healthy young individuals, heat illness is frequently the result of failure to make the necessary behavioral responses to heat strain, owing either to excessive motivation or to improper supervision.

Balance Between Heat Production and Heat Loss

Although the body exchanges some energy with the environment in the form of mechanical work, most is exchanged as heat by conduction, convection, and radiation and as latent heat through evaporation or (rarely) condensation of water (Figure 104-2). If the sum of energy production and energy gain from the environment does not equal energy loss, the extra heat is "stored" in, or lost from, the body. This is summarized in the heat balance equation

$$M = E + R + C + K + W + S \qquad (104\text{-}1)$$

where M is the metabolic rate; E is the rate of heat loss by evaporation; R and C are rates of heat loss by radiation and convection, respectively; K is the rate of heat loss by conduction (only to solid objects in practice, as explained later); W is the rate of energy loss as mechanical work; and S is the rate of heat storage in the body (15,16), which is positive when body temperature is increasing.

Metabolic Rate and Sites of Heat Production

At thermal steady state, the rate of heat production in the body is equal to the rate of heat loss to the environment, and can be measured precisely by direct calorimetry, a rather cumbersome technique in which all heat and water vapor leaving the body are captured and measured using special apparatus. More usually, metabolic rate is estimated by *indirect calorimetry* (17) from measurements of O_2 consumption, since virtually all energy available to the body depends ultimately on oxygen-consuming chemical reactions. The heat production associated with consumption of 1 liter of O_2 varies somewhat with the fuel—carbohydrate, fat, or protein—that is oxidized. An average value of 20.2 kJ (4.83 kcal) per liter of O_2 is often used for metabolism of a mixed diet. Since the ratio of CO_2 produced to O_2 consumed varies according to the fuel, indirect calorimetry can be made more accurate by also measuring CO_2 production and calculating the amount of protein oxidized from urinary nitrogen excretion.

Metabolic rate at rest is approximately proportional to body surface area. In a fasting young man it is about 45 W/m^2 (81 W or 70 kcal/hr for 1.8 m^2 of body surface area, corresponding to an O_2 consumption of about 240 mL/min). At rest the trunk viscera and brain account for about 70% of energy production, even though they comprise only about 36% of the body mass (Table 104-1). During exercise, however, the muscles are the chief site of energy production,

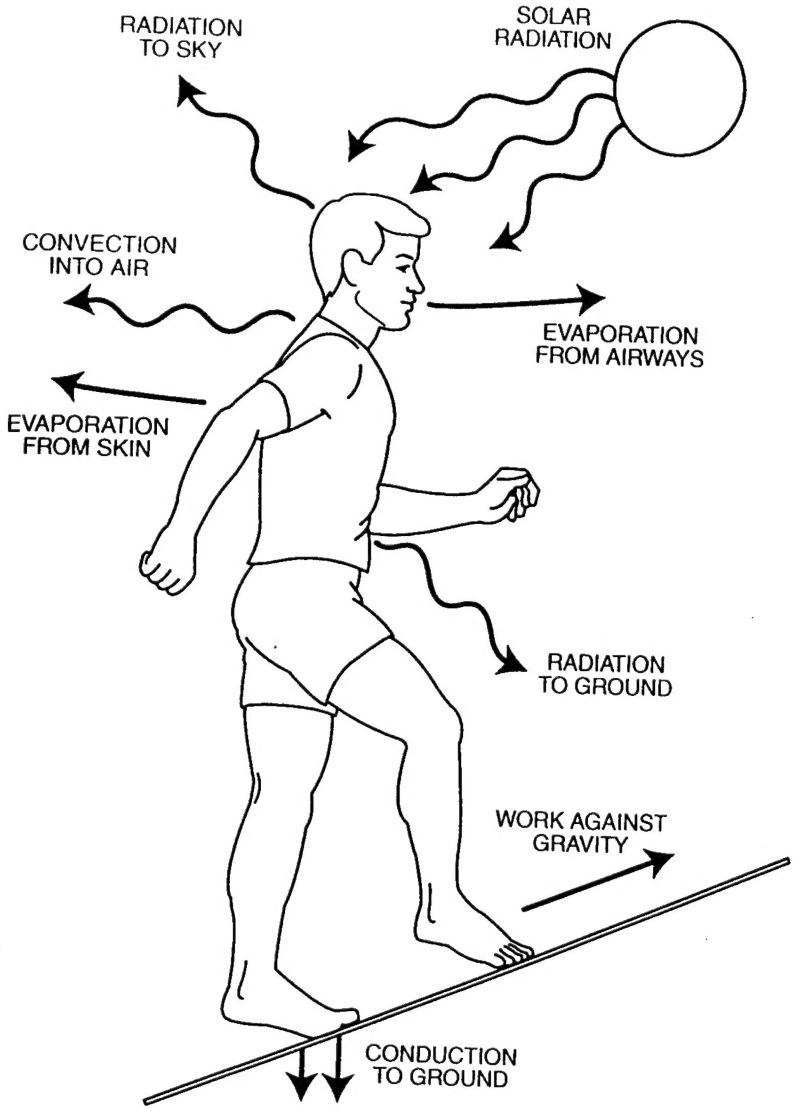

Figure 104-2 Exchange of energy with the environment. This hiker gains heat from the sun by radiation, and loses heat by conduction to the ground through the soles of his feet, by convection into the air, by radiation to the ground and sky, and by evaporation of water from his skin and respiratory passages. In addition, some of the energy released by his metabolic processes is converted into mechanical work, rather than heat, since he is walking uphill. (Redrawn from Wenger CB: The regulation of body temperature. In: Rhoades RA, Tanner GA, eds. Medical physiology. Boston: Little, Brown, 1995:587–613, with permission of the publisher.)

and may account for 90% during heavy exercise (Table 104-1). A healthy but sedentary young man performing moderate exercise may reach a metabolic rate of 600 W, and a trained athlete performing intense exercise may reach 1400 W or more. The overall mechanical efficiency of exercise varies enormously, depending on the activity; at best, no more than one quarter of the metabolic energy is converted into mechanical work outside the body, and the remaining three quarters or more is converted into heat within the body (18). Since exercising muscles produce so much heat, they may be nearly 1°C warmer than the core. They warm the blood that perfuses them, and this blood, returning to the core, warms the rest of the body.

Biophysics of Heat Exchange with the Environment

Radiation, convection, and evaporation are the dominant means of heat exchange with the environment. In humans, respiration usually accounts for only a minor fraction of total

Table 104-1 Relative Masses and Rates of Metabolic Heat Production of Various Body Compartments During Rest and Severe Exercise

	Body Mass (%)	Heat Production (%)	
		Rest	Exercise
Brain	2	16	1
Trunk Viscera	34	56	8
Muscle and Skin	56	18	90
Other	8	10	1

Modified from Wenger CB, Hardy JD. Temperature regulation and exposure to heat and cold. In: Lehmann JF, ed. Therapeutic heat and cold. 4th ed. Baltimore: Williams & Wilkins, 1990:150–178.

heat exchange and is not predominantly under thermoregulatory control, although hyperthermic subjects may hyperventilate. Therefore, humans exchange the most heat with the environment through the skin, and the rate of heat exchange between the body and the environment depends on the surface area of the skin.

Every surface emits energy as electromagnetic radiation with a power output that depends on its area, reflectivity, and temperature. Every surface absorbs electromagnetic radiation from its environment at a rate that depends on its area and reflectivity, and on the radiant temperature of the environment (T_r). Radiative heat exchange (R) between the skin and the environment is proportional to the difference between the fourth powers of the surfaces' respective absolute temperatures; however, if the difference between skin temperature (T_{sk}) and T_r is much smaller than the absolute temperature of the skin, R is approximately proportional to ($T_{sk} - T_r$). At ordinary tissue and environmental temperatures, virtually all radiant energy is in the far infrared range, where nearly all surfaces except polished metals have low reflectivities. However, bodies like the sun that are hot enough to glow emit large amounts of radiation in the near infrared and visible range, in which light-colored surfaces have higher reflectivities than dark ones. The practical importance of this is that skin and clothing color have little effect on heat exchange except in sunlight or intense artificial light.

Convection is the transfer of heat via a moving fluid, either liquid or gas. In thermal physiology the fluid is usually air or water in the environment, or blood inside the body, as discussed later in the chapter. Fluids conduct heat in the same way as solids do, and a perfectly still fluid transfers heat only by conduction. Since air and water are not good conductors of heat, perfectly still air or water is not very effective in heat transfer. Fluids, however, are rarely perfectly still, and even nearly imperceptible movement produces enough convection to have a large effect on heat transfer. Thus, although conduction plays a role in heat transfer by a fluid, convection so dominates the overall heat transfer that we refer to the entire process as convection. Therefore, the conduction term (K) in Equation (104-1) is in practice restricted to heat flow between the body and other solid objects, and usually represents only a small part of the total heat exchange with the environment. Convective heat exchange between the skin and the ambient air is proportional to the skin surface area and the difference between skin and air temperatures. Convective heat exchange depends also on geometrical factors that affect heat exchange with moving air, and on the degree of air movement. It is approximately proportional to the square root of air speed, except when air movement is very slight.

A gram of water that is converted into vapor at 30°C absorbs 2425 J (0.58 kcal) in the process. In subjects who are not sweating, evaporative water loss is typically about 13 to 15 g/(m^2·hr), corresponding to a heat loss of 16 to 18 W for a surface area of 1.8 m^2. About half of this amount is lost through breathing and half as *insensible perspiration* (19,20) (i.e., evaporation of water that diffuses through the skin). Insensible perspiration is unrelated to the sweat glands and is not under thermoregulatory control. These modes of water loss, however, are quite small compared to sweating. Evaporation of sweat from the skin is proportional to the skin surface area that is wet with sweat, and depends also on air movement, since water vapor is carried away by moving air, and on the temperature of the skin and the moisture content of the air. The most familiar way of expressing the moisture content of the air is the relative humidity, which is the ratio between the actual moisture content of the air and the maximum moisture content that is possible at the temperature of the air. However, relative humidity is not the most useful measure of the evaporative cooling power of the environment for thermal physiology, and may be misleading. A more useful index is the wet-bulb temperature, which is the temperature of a completely wet ventilated surface that is not artificially heated or cooled, and may be measured with a psychrometer. The temperature inside a closed vehicle or poorly ventilated building in direct sunlight may easily reach 50°C (122°F); if there are sources of moisture inside, the relative humidity may reach 37%—which may not sound particularly high. However the wet-bulb temperature in such an environment is 35°C (95°F), the same as in a 35°C environment at 100% relative humidity.

Tissue Blood Flow and Heat Transport in the Body

Heat travels within the body by two parallel means: *conduction* through the tissues and *convection* by the blood, the process by which flowing blood carries heat from warmer to cooler tissues. Heat flow by conduction is proportional to the change of temperature with distance in the direction of heat flow, and to the thermal conductivity of the tissues. Heat flow by convection depends on the rate of blood flow through the tissue and the temperature difference between the tissue and the blood supplying it. The power of the body to transport heat through a layer of tissue by conduction and convection combined is expressed as a quantity called *conductance*, C, defined as $C = HF/(\Delta T)$, where HF is the rate of heat flow through the tissue layer, and ΔT is the temperature difference across the tissue layer.

The most important conductance for thermal physiology is that involved in heat transfer from body core to skin. The skin and other superficial and peripheral tissues are, in general, cooler than the core. These cooler tissues, lying between the core and the skin surface, comprise the shell. (The shell is defined functionally rather than anatomically, and is thinnest when the body is warm and skin blood flow is high.) Since all heat leaving the body via the skin passes through the shell, the shell insulates the core from the environment. In a cold subject, vasoconstriction reduces skin blood flow so much that the conductance of the shell, and thus core-to-skin heat transfer, is dominated by conduction. A representative value for shell conductance of a lean man under these conditions is 8.9 W/(m^2·°C), or about 16 W/°C for a whole body with a typical surface area of 1.8 m^2. The subcutaneous fat layer adds to the insulation value of the shell of a vasoconstricted subject, because it increases the thickness of the shell and has a conductivity only about 0.4 times that of dermis or muscle. In a warm subject, however, the shell is relatively thin and provides little insulation. Furthermore a warm subject's skin blood flow is high, so that heat flow from the core to the skin is dominated by convection. In these circumstances the subcutaneous fat layer—which affects conduction but not convection—has little effect on heat flow. (Obese individuals do tend to be less heat-tolerant than thinner individuals. However, the major reasons for this difference are first, that the obese are at a relative disadvantage for dissipating heat because they have less skin surface

area in proportion to their weight than do their thinner counterparts, and second, obese individuals tend to be less physically fit and thus, as discussed later, to have less well-developed thermoregulatory responses.)

Let us return to our vasoconstricted man with a shell conductance of 16 W/°C. Under these conditions a temperature difference between core and skin of 5°C allows a typical resting metabolic heat production of 80 W to be conducted to the skin surface. In a cool environment, T_{sk} may be low enough for this to occur easily. However in a warm environment or, especially, during exercise, shell conductance must increase substantially to allow all the heat produced to be conducted to the skin without at the same time causing core temperature to rise to dangerous or lethal levels. [For example without an increase in shell conductance, T_r (core temperature) would have to be 30°C higher than T_{sk} to allow a heat production of 480 W during moderate exercise to be carried to the skin.] Fortunately, under such circumstances increases in skin blood flow occur that can raise shell conductance tenfold or more. Thus, a crucial thermoregulatory function of skin blood flow is to control the conductance of the shell and the ease with which heat travels from core to skin. A closely related function is to control T_{sk}; in a person who is not sweating, an increase in skin blood flow tends to bring T_{sk} toward T_r, and a decrease allows T_{sk} to approach ambient temperature. Since convective and radiative heat exchange ($R + C$) depend directly on skin temperature, the body can control heat exchange with the environment by adjusting skin blood flow. If the heat stress is so great that increasing R + C through increasing skin blood flow is not enough to maintain heat balance, the body secretes sweat to increase evaporative heat loss. Once sweating begins, skin blood flow continues to increase as the person becomes warmer, but now the tendency of an increase in skin blood flow to warm the skin is approximately balanced by the tendency of an increase in sweating to cool the skin. Therefore, after sweating has begun, further increases in skin blood flow usually cause little change in skin temperature or dry heat exchange. Nevertheless, the increases in skin blood flow that accompany sweating are important to thermoregulation, since they deliver to the skin the heat that is being removed by evaporation of sweat, and facilitate evaporation by keeping the skin warm. Skin blood flow and sweating thus work in tandem to dissipate heat that is produced in the body.

Physiologic Heat-Dissipating Responses

Responses of Skin Vascular Beds, and Pooling of Blood

Blood vessels in human skin are under dual vasomotor control, involving separate nervous signals for vasoconstriction and for vasodilation (21–23). Reflex vasoconstriction, occurring in response to cold and also as part of certain nonthermal reflexes such as baroreflexes, is mediated primarily through adrenergic sympathetic fibers distributed widely over most of the skin (24). Reducing the flow of impulses in these nerve fibers allows the blood vessels to dilate. In the so-called acral regions—lips, ears, nose, palms of the hands, and soles of the feet (23,24)—and in the superficial veins (23), vasoconstrictor fibers are the predominant vasomotor innervation, and the vasodilation occurring during heat exposure is largely a result of withdrawal of vasoconstrictor activity (25). Reflex control of skin blood flow in these regions, unlike that in the rest of the skin (25), is sensitive to small temperature changes in the thermoneutral range (i.e., the range of thermal conditions in which the body is neither chilled nor sweating) and may "fine tune" heat loss to maintain heat balance in this range.

In most of the skin the vasodilation occurring during heat exposure depends on sympathetic nervous signals that cause the blood vessels to dilate, and is prevented or reversed by regional nerve block (26). Since it depends on the action of nervous signals, such vasodilation is sometimes referred to as *active* vasodilation. Active vasodilation occurs in almost all the skin outside the acral regions (25). In skin areas where active vasodilation occurs, vasoconstrictor activity is minimal in the thermoneutral range; as the body is warmed, active vasodilation does not begin until near the onset of sweating (23,27). The neurotransmitter or other vasoactive substance(s) responsible for active vasodilation in human skin is not known (24). However, since sweating and vasodilation operate in tandem in the heat, there has been considerable interest in the notion that the mechanism for active vasodilation is somehow linked to the action of sweat glands (23,28). Active vasodilation does not occur in the skin of patients with anhidrotic ectodermal dysplasia (29), even though their vasoconstrictor responses are intact, implying that active vasodilation either is linked to an action of sweat glands, or is mediated through nerves that are absent or nonfunctional in anhidrotic ectodermal dysplasia.

The superficial venous beds, which receive blood from the skin, are fully dilated at mild levels of heat stress. Therefore, in regions below the level of the heart, these veins readily become engorged with blood, especially when skin blood flow is high, and the resulting peripheral pooling of blood impairs venous return, reduces central blood volume, compromises diastolic filling of the heart, and limits cardiac output, especially during exercise. The most important physiologic compensatory mechanism is constriction of the renal and splanchnic vascular beds. Reduction of blood flow through these beds increases the fraction of cardiac output that is available to perfuse exercising muscle. In addition, the splanchnic vascular bed is very compliant, so that a reduction in splanchnic blood flow reduces the volume of blood contained in the splanchnic vascular bed, allowing a partial restoration of central blood volume and cardiac diastolic filling. The effect of pooling of blood in the skin on central blood volume, and the compensatory effect of splanchnic vasoconstriction are shown schematically in Figure 104-3. The degree of splanchnic vasoconstriction is graded according to the levels of heat stress and exercise intensity. During strenuous exercise in the heat, renal and splanchnic blood flows may fall to 20% of their values in a cool resting subject (23,30). Such intense splanchnic vasoconstriction may help to explain the intestinal symptoms that some athletes experience after endurance events (31).

Sweating and Loss of Fluid and Electrolytes

Humans can dissipate large amounts of heat by secretion and evaporation of sweat, and when the environment is warmer than the skin—usually when the environment is warmer than about 35°C—evaporation is the only way to lose heat. Human sweat glands are controlled through postganglionic sympathetic nerves that release acetylcholine (32) rather than

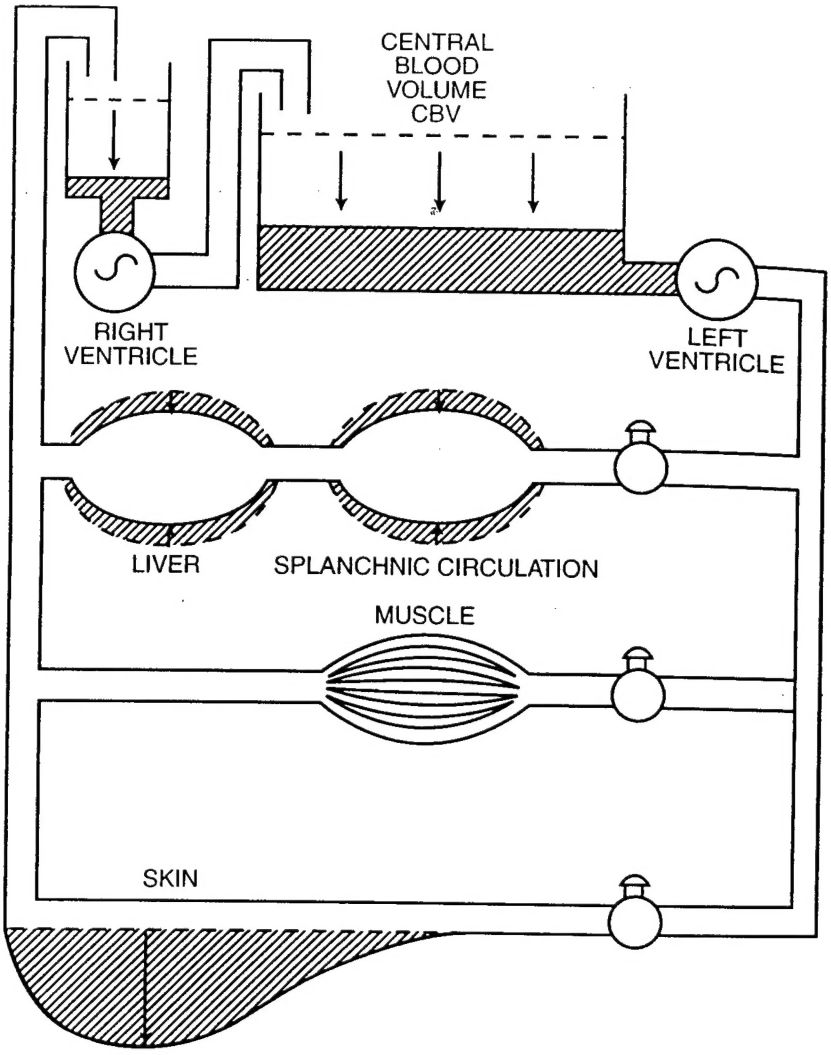

Figure 104-3 Schematic diagram of the effects of skin vasodilation on peripheral pooling of blood and the thoracic reservoirs from which the ventricles are filled, and also the effects of compensatory vasomotor adjustments in the splanchnic circulation. The valves drawn at the right sides of liver/splanchnic, muscle, and skin vascular beds represent the resistance vessels that control blood flow through those beds. Arrows show the direction of the changes during heat stress. (Redrawn from Rowell LB. Cardiovascular adjustments to thermal stress. In: Shepherd JT, Abboud FM, eds. Handbook of physiology. The cardiovascular system. Peripheral circulation and organ blood flow. Bethesda, MD: American Physiological Society, 1983:sect. 2, vol. 3, 967–1023; and Rowell LB. Cardiovascular aspects of human thermoregulation. Circ Res 1983;52:367–379.)

norepinephrine like most other sympathetic nerves. Human skin contains 2 to 3 million functional eccrine sweat glands (32), the histologic type most important in thermoregulation. Their secretory capacity can be increased by aerobic exercise training and heat acclimatization; a fit man well acclimatized to heat can achieve a peak sweating rate greater than 2.5 liters per hour (33,34). Such rates cannot long be maintained, however, and the maximum daily sweat output is probably about 15 liters (35).

Eccrine sweat is formed from a precursor fluid in the secretory coil of the gland. This fluid is initially isotonic with plasma; however, as it moves along the duct, Na^+ is reabsorbed from the fluid by active transport. When it emerges from the duct as sweat, it is the most dilute body fluid, with $[Na^+]$ ranging from less than 5 to 60 mEq/L (36). As the rate of sweat secretion increases, the precursor fluid moves through the duct more quickly, so that a smaller fraction of its initial sodium content is reabsorbed, and $[Na^+]$ in the resulting sweat is higher. Thus salt losses through sweating increase disproportionately as sweat production rises.

At high sweating rates, large volumes of water can be lost in a few hours, and the consequent reduction in plasma volume may compromise cardiovascular homeostasis and cardiac output. In addition, since sweat is hypotonic to plasma, loss of sweat progressively increases the osmolality of the bodily fluids if the water is not replaced. Both the reduction in plasma volume and the increase in osmolality will compromise thermoregulation by shifting the thresholds for sweating and vasodilation in the skin toward higher core temperature. If large amounts of salt are lost, and only the water but not the salt is replaced, plasma volume will not return to normal because the loss of salt reduces the total number of osmoles in the extracellular fluid, so that the water that is replaced goes preferentially into the intracellular space.

During prolonged (several hours) heat exposure with high sweat output, sweat rates gradually diminish and the sweat glands' response to locally applied cholinergic drugs is reduced also. The reduction of sweat-gland responsiveness is sometimes called sweat-gland "fatigue." One mechanism involved is hydration of the stratum corneum, which swells and mechanically obstructs the sweat duct, causing a reduction in sweat secretion, an effect called *hidromeiosis* (37). The glands' responsiveness can be at least partly restored if the skin is allowed to dry [e.g., by increasing air movement (38)], but prolonged sweating also causes histologic changes in the sweat glands (39).

Control of Thermoregulatory Responses

Integration of Thermal Information

Temperature receptors in the body core and the skin transmit information about their temperatures through afferent nerves to the brain stem, and especially the hypothalamus, where much of the integration of temperature information takes place. Although temperature receptors in other core sites, including the spinal cord and medulla, participate in the control of thermoregulatory responses (40); the core temperature receptors involved in thermoregulatory control are concentrated especially in the hypothalamus (40); temperature changes of only a few tenths of 1°C in the anterior preoptic area of the hypothalamus elicit changes in the thermoregulatory effector responses of experimental mammals.

Most physiologic control systems produce a response that is graded according to the disturbance in the regulated variable. In many of these systems, including those that control the heat-dissipating responses, changes in the effector responses are proportional to displacements of the regulated variable from some threshold value (19); such control systems are called *proportional control* systems. Changes in the heat-dissipating responses are proportional to displacements of core temperature from some threshold value (Figure 104-4). Each response in Figure 104-4 has a core-temperature threshold, a temperature at which the response starts to increase; these thresholds depend on mean skin temperature. Thus, at any given skin temperature, the change in each response is proportional to the change in core temperature; increasing the skin temperature lowers the threshold level of core temperature and increases the response at any given core temperature. (Control of the heat-dissipating responses is more complicated than a basic proportional-control system, since these responses are controlled according to both core and skin temperature.) The sensitivity of the thermoregulatory system to core temperature allows it to adjust heat loss so as to resist disturbances in core temperature, and the system's sensitivity to skin temperature allows it to respond appropriately to moderate changes in the environment with little or no change in body core temperature. For example, the skin temperature of someone who enters a hot environment rises and may elicit sweating even if there is no change in core temperature. On the other hand, an increase in heat production due to exercise elicits the appropriate heat-dissipating responses through a rise in core temperature.

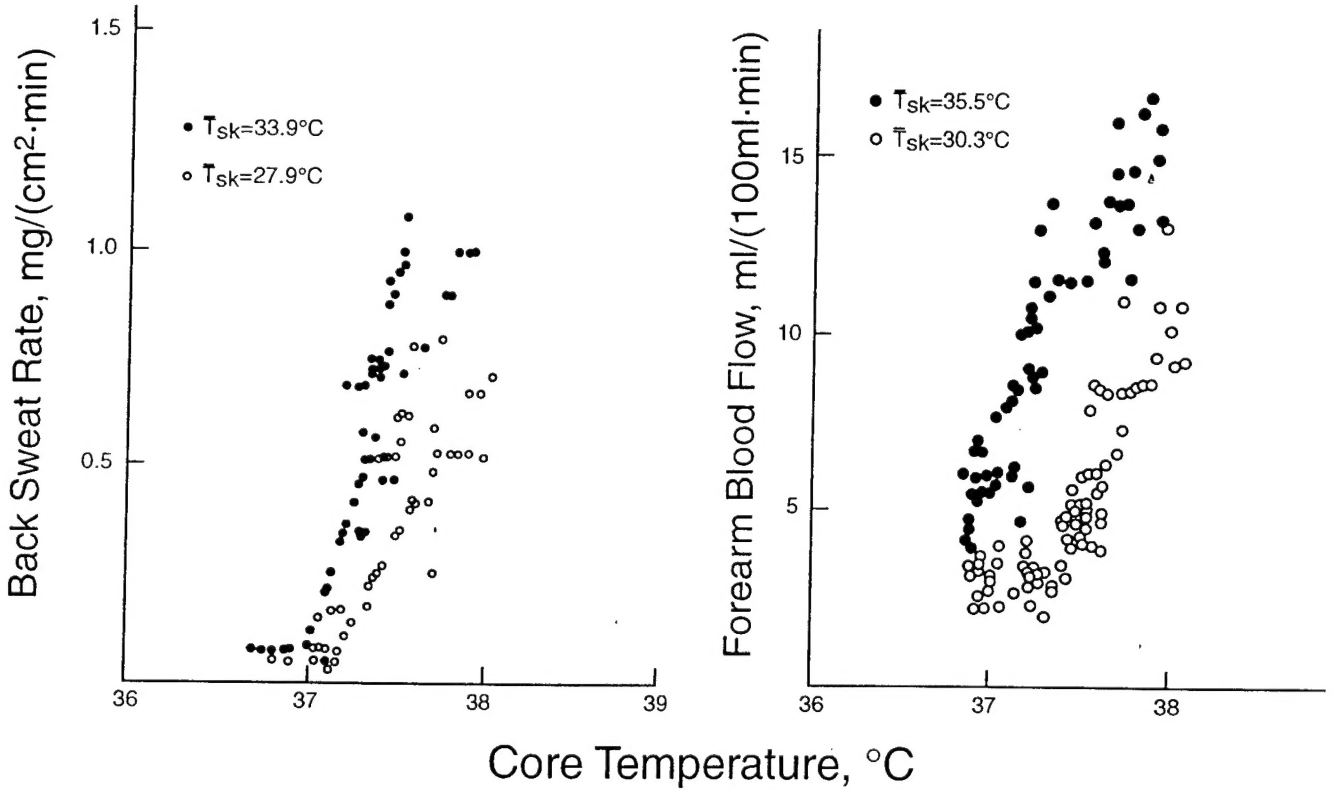

Figure 104-4 The relationships of back sweat rate (left) and forearm blood flow (right) to esophageal and mean skin temperatures (T_{es} and T_{sk}). Sweating data are from four subjects performing cycle exercise at an O_2 consumption rate of 1.6 L/min. Blood flow data are from one subject. During measurements of blood flow, forearm temperature was kept at 36.8°C to eliminate a difference in local temperature between experiments. Local temperature was not controlled independently during measurements of sweating, so that the difference between conditions includes a small effect of local skin temperature, appearing as a difference in slope. (Left panel drawn from data of Sawka MN, Gonzalez RR, Drolet LL, Pandolf KB. Heat exchange during upper- and lower-body exercise. J Appl Physiol 1984;57:1050–1054; right panel modified from Wenger CB, Roberts MF, Stolwijk JAJ, Nadel ER. Forearm blood flow during body temperature transients produced by leg exercise. J Appl Physiol 1975;38:58–63.)

Both sweating and skin blood flow participate in other reflexes besides thermoregulatory responses. For the purposes of this chapter, the most important nonthermoregulatory reflexes are those that involve the blood vessels of the skin in responses that help to maintain cardiac output, blood pressure, and tissue O_2 delivery. During heat stress, thermoregulatory requirements usually dominate the control of these responses, but in conditions of high cardiovascular strain thermoregulatory requirements for skin blood flow may be overridden to support circulatory function. An important and dramatic example is the reduction in skin blood flow that accounts for the cool, ashen skin characteristic of heat exhaustion, discussed below.

Thermoregulatory Responses During Exercise

At the start of exercise, metabolic heat production increases rapidly; however, there is little change in heat loss initially, so heat is stored in the body and core temperature rises. The increase in core temperature, in turn, elicits heat-loss responses, but core temperature continues to rise until heat loss has increased enough to match heat production, so that heat balance is restored and core temperature and the heat-loss responses reach new steady-state levels. The rise in core temperature that elicits heat-dissipating responses sufficient to re-establish thermal balance during exercise is an example of a *load error* (19), which occurs when any proportional control system resists the effect of some imposed disturbance or "load." The load error is proportional to the load, so that the elevation in core temperature during exercise is proportional to the rate of heat production. Although the elevated core temperature during exercise superficially resembles that during fever due to resetting of the body's thermostat, there are some crucial differences. First, although heat production may increase substantially (through shivering) at the beginning of a fever, it does not need to stay high to maintain the fever, but in fact returns nearly to prefebrile levels once the fever is established; during exercise, however, an increase in heat production not only causes the elevation in core temperature, but is necessary to sustain it. Second, the rate of heat loss while core temperature is rising during a fever, is, if anything, lower than before the fever began, but the rate of heat loss during exercise starts to increase as soon as core temperature starts to rise and continues to increase as long as core temperature is rising.

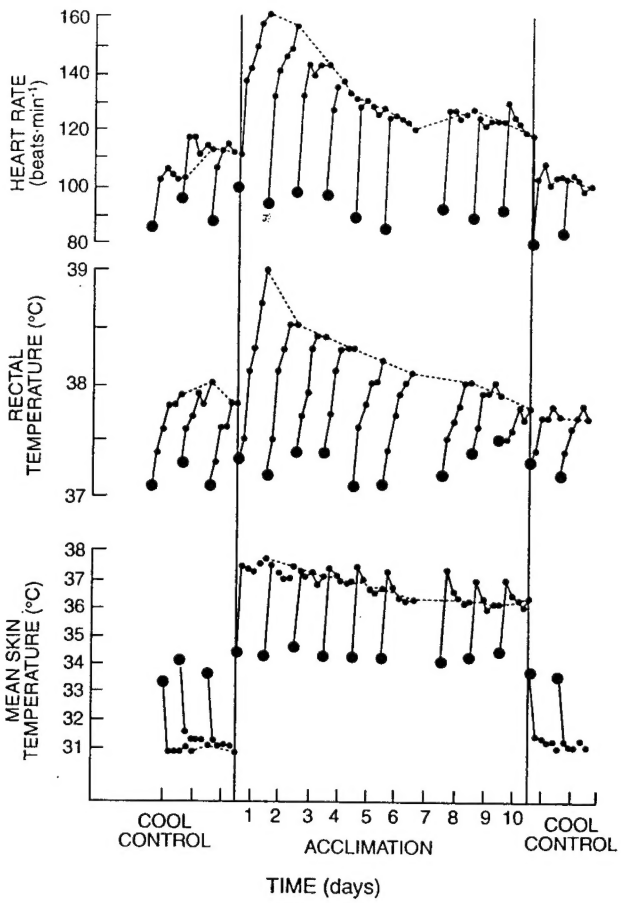

Figure 104-5 Change in the responses of heart rate, rectal temperature, and mean skin temperature during exercise in a 10-day program of acclimatization to dry heat (50.5°C, 15% relative humidity), together with responses during exercise in a cool environment before and after acclimatization. (The "cool control" condition was 25.5°C, 39% relative humidity.) Each day's exercise consisted of five 10-minute treadmill walks at 2.5 mph (1.12 m/s) up a 2.5% grade. Successive walks were separated by 2-minute rest periods. Large circles show values before the start of the first exercise period each day, small circles show values at the ends of successive exercise periods, and dotted lines connect final values each day. (Redrawn from Eichna LW, Park CR, Nelson N, et al. Thermal regulation during acclimatization in a hot, dry (desert type) environment. Am J Physiol 1950;163:585–597.)

FACTORS AFFECTING HEAT TOLERANCE

Acclimatization and Physical Fitness

Prolonged or repeated heat stress, especially when combined with exercise sufficient to elicit profuse sweating, produces *acclimatization* to heat (41), a set of physiologic changes that reduces the physiologic strain associated with exercise-heat stress. The classic signs of heat acclimatization are reductions in the levels of core and skin temperatures and heart rate, and increases in sweat production during a given level of exercise in the heat. These changes begin to appear during the first few days and approach their full development within a week. Figure 104-5 illustrates some of these effects in three young men who were acclimatized by daily treadmill walks in dry heat for 10 days (42). On the first day in the heat, heart rate and rectal temperature during exercise reached much higher levels than in cool control (25°C) conditions; however, on the tenth day in the heat, final heart rate and rectal temperature during exercise were 40 beats/min and 1°C, respectively, lower than on the first day. In addition, sweat production increased 10%, skin temperature was about 1.5°C lower, and the metabolic cost of treadmill walking decreased 4%. The mechanisms that produce these changes are not fully understood, but include a modest (~0.4°C) reduction in the setting

of the body's thermostat (thus reducing the thresholds for sweating and cutaneous vasodilation), increased sensitivity of the sweat glands to cholinergic stimulation (43,44), a decrease in the sweat glands' susceptibility to hidromeiosis and fatigue, and retention of salt and water and expansion of plasma volume to compensate for peripheral pooling of blood in dilated blood vessels in the skin. Heat acclimatization produces other changes (41) also, including an improved ability to sustain high rates of sweat production; an aldosterone-mediated reduction of sweat sodium concentration (to levels as low as 5 mEq/L at low sweat rates), which minimizes salt depletion; an increase in the fraction of sweat secreted on the limbs; and perhaps other changes that help protect against heat illness. The effect of heat acclimatization on performance can be quite dramatic, so that acclimatized subjects can easily complete exercise in the heat that previously was difficult or impossible (see Reference 45). The benefits of acclimatization are lessened or reversed by sleep loss, infection, alcohol abuse, dehydration, and salt depletion (41). Heat acclimatization disappears in a few weeks if not maintained by repeated heat exposure.

Some of the changes that occur with heat acclimatization are mediated by "training" the heat-dissipating responses, particularly sweating, through repeated use (41). Repeated aerobic exercise of sufficient intensity and duration to improve maximal O_2 consumption also trains the heat-dissipating responses and expands plasma volume, and produces an improvement in heat tolerance similar to that associated with heat acclimatization (41). This effect probably explains the association of physical fitness with heat tolerance.

Gender, Age, Obesity, Drugs, and Skin Disorders

Although women as a group are less tolerant to exercise-heat stress than men, the difference appears to be explained by differences in size, acclimatization, and maximal O_2 consumption; when subjects are matched according to these variables, gender differences largely disappear (46). Curiously, the exertional form of heat stroke is quite rare in women (13), but it is unknown whether the explanation for its rarity is biological or behavioral. The effect of phase of the menstrual cycle has not been well studied. However Pivarnik et al (47), studying women's responses during cycle exercise at 22°C, found that after 60 minutes of exercise heart rate was 10 beats/min higher in the luteal than in the follicular phase; rectal temperature increased 1.2°C in the luteal phase and was still rising, whereas it increased 0.9°C in the follicular phase and was near steady state. Although they examined only one set of experimental conditions, using a temperate rather than a warm environment, their data suggest a decline in tolerance to exercise-heat stress during the luteal phase.

The effectiveness of the thermoregulatory system is reduced with increasing age, but it is not clear how much of the decrease is a direct effect of aging itself, and how much owes to changes that tend to accompany increased age, such as reduced physical fitness (46). Obesity also is associated with reduced heat tolerance, and Kenney (46) reviews mechanisms that may explain this association. Thermoregulation is also impaired by salt and water depletion, and by a number of drugs, including diuretics, which may cause loss of fluid and electrolytes, and various drugs that suppress sweating, including anticholinergics, antiparkinsonians, antihistamines, and phenothiazines (11). In addition some drugs, including tricyclic antidepressants, butyrophenones, and amphetamines, increase the risk of heat illness through other mechanisms (11).

Several congenital and acquired skin disorders impair sweating, and may greatly reduce heat tolerance. Anhidrotic ectodermal dysplasia is especially interesting in this regard, since not only sweating, but also active vasodilation in the skin, is impaired or absent. Thus artificially wetting the skin only partially corrects the thermoregulatory deficit during exercise, when large amounts of body heat need to be carried to the skin. Artificial wetting is probably most effective in a dry environment, in which evaporation can produce a cool skin.

ADVERSE EFFECTS OF HEAT AND EXERCISE

Although hyperthermia is often associated with heat disorders, and may be involved in the pathogenesis, the relation between body temperature and clinical manifestations is complex (48), and levels of core temperatures that are typically associated with heat stroke have been observed in athletes who apparently suffered no ill effects (49,50). For convenience the heat disorders may be divided into two groups: those whose manifestations are primarily local, and those having more general manifestations. This division is not absolute, however, since miliaria rubra may impair thermoregulation.

For more detailed discussion of pathogenesis and clinical management the reader is referred elsewhere (11,13).

Heat Disorders

Disorders with Primarily Local Manifestations

Heat edema, a dependent edema of the hands, legs, and feet, typically occurs within the first week of adaptation to tropical heat, and is worsened by prolonged standing. Heat edema is probably due to the retention of salt and water that is a normal part of acclimatization to heat, and peripheral vasodilation probably has a contributory role. Heat edema is a benign and self-limited condition. Treatment with diuretics is not indicated and will impair development of acclimatization by interfering with retention of salt and water.

Miliaria rubra (commonly called heat rash or prickly heat) is characterized by blockage of the sweat ducts with plugs of keratin debris, and typically occurs following repeated or prolonged exposure to heat. The resulting rash is irritating, but the most serious effect is marked impairment of sweating in the affected skin, which may precede the appearance of the rash by up to a week and may persist for some time after the rash clears (51). Some patients may be unable to sweat below the neck. The impairment of sweating, if extensive, substantially limits the ability to tolerate exercise in the heat.

Heat Syncope

Heat syncope is a temporary circulatory failure due to pooling of blood in the peripheral veins and a consequent decrease in diastolic filling of the heart. The primary cause of the

peripheral pooling is the large increase in skin blood flow that occurs as part of the thermoregulatory response to heat exposure, but an inadequate baroreflex response may be an important contributing factor. It usually occurs in individuals who are standing with little activity. Symptoms may range from lightheadedness to loss of consciousness. Core temperature typically is no more than slightly elevated except when an attack follows exercise, and the skin is wet and cool. Recovery is rapid once the patient sits or lies down, although complete recovery of blood pressure and heart rate often takes an hour or two. Heat syncope affects mostly those who are not acclimatized to heat, presumably because the expansion of plasma volume that occurs with acclimatization compensates for the peripheral pooling of blood. Patients being treated for hypertension with diuretics or medications that impair the baroreflexes are at particular risk, and should exercise care when standing in crowds or lines in hot surroundings.

The Continuum of Heat Cramps, Heat Exhaustion, and Heat Stroke

Traditionally heat cramps, heat exhaustion, and heat stroke were considered to be three distinct clinical entities. However these disorders have overlapping features, and the concept that they are syndromes representing different parts of a continuum (52,53) has gained favor. In keeping with this concept, some recent literature describes a syndrome called *exertional heat injury*, intermediate in severity between heat exhaustion and heat stroke. However, there does not seem to be a consensus on diagnostic criteria for distinguishing exertional heat injury from heat exhaustion on one hand or heat stroke on the other (compare, for example, References 54 and 55).

Water loss from the sweat glands can exceed 1 liter per hour during exercise in the heat. The amount of salt lost in the sweat is quite variable, and persons who are well acclimatized to heat can often secrete very dilute sweat. However, those who are less well acclimatized may lose large amounts of salt in their sweat and become substantially salt-depleted.

Heat Cramps

Heat cramps is an acute disorder consisting of brief, recurrent, and often agonizing cramps in skeletal muscles of the limbs and trunk. The cramp produces a hard lump in the affected muscle, which typically has recently participated in intense exercise. Although the cramps are brief, generally lasting only a few minutes, they may recur for many hours in severe, untreated cases. Patients are characteristically physically fit men, well acclimatized to heat, who have been drinking adequate amounts of water but not replacing salt lost in the sweat. They are usually hyponatremic, and the hyponatremia is thought to be involved in the pathogenesis of the cramps, although the mechanism is obscure. Hyponatremia is rather common, however, whereas heat cramps are an unusual accompaniment. Intravenous infusion of 0.5 to 1 liter of normal saline, or alternatively, somewhat smaller amounts of hypertonic saline, is the treatment of choice in severe cases. However, administration by mouth of 0.1% salt in water is also effective (11), somewhat unexpectedly given the usual association of heat cramps with hyponatremia. The immediate goal of treatment is relief of the cramps, not restoration of salt balance, which takes longer and is best achieved by giving salted food or fluids by mouth.

Heat Exhaustion

Heat exhaustion is characterized by circulatory collapse occurring after prolonged or repeated exercise-heat stress. Most patients have lost both salt and water, but heat exhaustion may be associated either predominantly with salt depletion or predominantly with water depletion. Salt-depleted patients are hypovolemic out of proportion to the degree of dehydration (and are hypovolemic even if not greatly dehydrated), since their body water is distributed preferentially to the intracellular space in order to maintain osmotic balance between the intra- and extracellular spaces. They tend either to be unacclimatized to heat or to be consuming small amounts of salt in their diet, and they have replaced at least some of their water loss. Heat exhaustion caused primarily by water depletion tends to develop more rapidly than that caused by salt depletion, and is characterized by greater thirst. In addition, hypovolemia occurring during water-depletion heat exhaustion is associated with less hemoconcentration, since water is lost from both the red cells and the plasma.

Heat exhaustion spans a clinical spectrum from fairly mild disorders that respond well to rest in a cool environment and fluid replacement by mouth to severe forms with collapse, confusion, and hyperpyrexia. Loss of consciousness is uncommon, but there may be vertigo, ataxia, headache, weakness, nausea, vomiting, pallor, tachycardia, and low blood pressure. The patient usually is sweating profusely. Muscle cramps indistinguishable from heat cramps may occur, especially if salt depletion is part of the pathogenesis. Treatment consists primarily of laying the patient down away from the heat and replacing fluid and salt, as needed. In severe cases, intravenous administration of normal saline may be required. Active cooling measures may be called for if the patient's core temperature is 40.6°C (105°F) or higher, since water-depletion heat exhaustion may lead to heat stroke.

Restoration of Fluid Loss

As $[Na^+]$ in the extracellular fluid is reduced, fluid moves from the extracellular fluid into the intracellular fluid to maintain osmotic balance, causing the cells to swell. Since the brain occupies most of the space within a rigid case, even a modest degree of cerebral edema can increase intracranial pressure, leading to encephalopathy and brain stem herniation in extreme cases. By removal of interstitial fluid and by loss of solutes from within the cells, the brain can protect itself from osmotic swelling if plasma $[Na^+]$ changes slowly enough (56). Although osmotic swelling of the brain is usually associated with hyponatremia, its occurrence is related to the rate of change of plasma $[Na^+]$ rather than the level of $[Na^+]$. For this reason care should be taken to avoid reducing plasma $[Na^+]$ too rapidly when replacing water in water-depleted patients (11). In addition, a few individuals who are drinking large amounts of fluid during sustained exercise in the heat may become hyponatremic if they lose excessive amounts of salt in their sweat or drink and retain more fluid than is required to replace their losses (57–59). Although this condition is far less common than water-depletion heat exhaustion, it may be difficult to distinguish the two conditions from each

other in the early stages without laboratory tests. Patients with water-depletion heat exhaustion respond rather quickly to fluid replacement, whereas hyponatremia is aggravated by administering hypotonic fluids, and may progress to life-threatening cerebral edema. Therefore, in a patient who was presumed to have heat exhaustion but does not improve quickly in response to administration of hypotonic fluids, such treatment should not be continued without further medical evaluation. (A rule suggested for field use is that a patient with presumed heat exhaustion should be given 2 quarts of water to drink over the course of an hour, and needs medical evaluation if noticeable improvement has not occurred by the end of the hour.)

Heat Stroke

Heat stroke is the most severe heat disorder and is characterized by rapid development of hyperthermia and severe neurologic disturbances, frequently including convulsions. Although these disturbances typically are characteristic of a nonfocal encephalopathy, some patients may show abnormalities of cerebellar function, which may be transient or may persist. Heat stroke may be complicated by liver damage, electrolyte abnormalities, and especially in the exertional form, by rhabdomyolysis, disseminated intravascular coagulation, or renal failure.

Loss of consciousness may occur suddenly, or may be preceded by up to an hour of prodromata, including headache, dizziness, drowsiness, restlessness, ataxia, confusion, and irrational or aggressive behavior. The physiologic pathology is not well understood, and there is some indication that factors other than hyperthermia contribute to the development of heat stroke. Heat stroke may be divided into two forms depending on the pathogenesis. In the classic form, the primary pathogenic factor is environmental heat stress that overwhelms an impaired thermoregulatory system, whereas in exertional heat stroke the primary factor is metabolic heat production. (See Reference 11 for a more extensive discussion.) Consequently, victims of the exertional form tend to be younger and physically fitter (typically soldiers, athletes, and laborers) than victims of the classic form. The traditional diagnostic criteria of heat stroke—coma, hot dry skin, and temperature above 41.3°C (106°F)—reflect experience primarily with the classic form. Adherence to these criteria will lead to underdiagnosis, since cessation of sweating may be a late event, especially in exertional heat stroke. Moreover, patients may come to medical attention either in the prodromal phase or after they have had a chance to cool somewhat and regain consciousness, especially if they still are sweating.

Measurements of rectal temperature or other deep body temperature are essential for clinical evaluation of hyperthermic patients and following response to treatment. A diagnosis of heat stroke must not be excluded on the basis either of oral temperature, or of temperature measured at the external auditory meatus or tympanic membrane. Because of hyperventilation, oral temperature may be 2 to 3°C lower than rectal temperature in heat stroke; the temperature of the external auditory meatus or tympanum may be as much as 5°C lower than rectal temperature in collapsed hyperthermic athletes (60). (Low values of the temperature of the tympanum may owe in part to cooling of its blood supply, which comes mostly from branches of the external carotid artery and thus follows a superficial course.) It is sometimes asserted that since the tympanum is so close to the cranium, tympanic temperature represents intracranial temperature—and thus the temperature of the brain—more accurately than any other noninvasive temperature measurement. Thus tympanic temperature measurements that are appreciably lower than measurements of trunk core (e.g., rectal or esophageal) temperature in hyperthermic human subjects are sometimes adduced to argue for the existence of physiologic heat-exchange mechanisms that protect the human brain during hyperthermia by cooling it below the temperature of the central blood. However, there is little empirical support either for the claims made for tympanic temperature or for the existence of special mechanisms to cool the human brain. (See References 28 and 61 for further discussion.)

Heat stroke is an extreme medical emergency, and prompt appropriate treatment is critically important in reducing morbidity and mortality. Cooling the patient to lower core temperature is the cornerstone of early treatment, and should begin as soon as possible. The patient should be removed from hot surroundings without delay, excess clothing and any equipment that obstructs free flow of air should be removed, the patient's skin should be wet if water is available, and the patient should be fanned to promote evaporative cooling. Although helpful, these measures are no substitute for more vigorous cooling once appropriate means are available, and cooling is accomplished most effectively by immersion in cold water. Costrini et al (62) lowered the rectal temperatures of their heat stroke patients at a mean rate of 0.18°C/min by immersing them in ice water. There is some disagreement as to the optimal water temperature, since lowering the temperature not only increases the core-to-skin thermal gradient for heat flow, but also reduces skin blood flow. Observations on heat-stroked dogs suggest that while 15 to 16°C (59 to 61°F) water is more effective than warmer water, little further advantage is gained with lower water temperatures (63). However there is no empirical support for the superiority of cooling methods, such as tepid baths or evaporation of sprayed water, that achieve only modest skin cooling. Some arguments in favor of such cooling methods are based on studies comparing different cooling methods in mildly hyperthermic normal subjects, whose peripheral vascular and other thermal responses may, however, be substantially different from those of heat stroke patients. The pitfalls in relying on such studies may be seen by comparing the following two reports: In tests on hot but normal young subjects, an evaporative cooling method was reported to be more effective than other cooling methods, causing tympanic temperature to fall at a rate of 0.31°C/min (64). However in a series of heat stroke patients the same authors found that the same cooling method lowered rectal temperature at a rate of only 0.06°C/min (65), one fifth the rate that they had reported in healthy individuals (64), and one third the rate that Costrini et al (62) achieved.

There is evidence for a systemic inflammatory component in heat stroke (53), and elevated levels of several inflammatory cytokines have been reported in patients presenting with heat stroke (66–68). Leakage of gram-negative endotoxin from the gut, perhaps facilitated by splanchnic ischemia, may be a trigger for secretion of these cytokines, since treatments aimed at preventing leakage of (69,70) or

neutralizing (71) endotoxin partially protect experimental animals against heat stroke during subsequent heating. Gaffin et al (72) have discussed the implications of these concepts for prevention and treatment of heat stroke, but the efficacy of their proposed measures has not been sufficiently tested to allow their recommendation.

Heat stroke is to be distinguished from malignant hyperpyrexia, a rare process provoked in genetically susceptible individuals by inhalational anesthetics or neuromuscular blocking agents (73). Reuptake of calcium ion by the sarcoplasmic reticulum is severely impaired so that concentrations in the cytoplasm rise, leading to an uncontrolled hypermetabolic process that produces a rapid rise in core temperature. Dantrolene sodium, which reduces release of calcium ion from the sarcoplasmic reticulum, is an effective treatment and has dramatically reduced the mortality rate of this disorder.

Aggravation of Other Diseases

Besides causing the more or less characteristic disorders discussed above, heat stress can worsen the clinical state of patients with a number of other diseases. For example, patients with congestive heart failure have substantially impaired sweating and circulatory responses to environmental heat stress, and exposure to moderately hot environments worsens the signs and symptoms of congestive heart failure (74). Conversely, air conditioning improves the clinical progress of patients hospitalized in the summer with a variety of cardiorespiratory and other chronic diseases (74). The harmful effects of heat stress on those suffering from other diseases are also shown by analysis of the effects of unusually hot weather on total mortality and causes of death. Ellis (75), in a study of U.S. Public Health Service vital statistics reports for the years 1952 to 1967, examined monthly mortality statistics for 5 "heat wave" years, defined as those having more than 500 deaths reported as caused by "excessive heat and insolation." June and July of the heat wave years had excess mortality (i.e., above that expected for the month) from diabetes; cerebrovascular accidents; arteriosclerotic, degenerative, and hypertensive heart disease; and diseases of the blood-forming organs. He estimated the total number of excess deaths was more than 10 times as great as the number of deaths actually reported as due to heat.

Epidemiologic studies of individual heat waves demonstrate the effects of heat stress even more strikingly. For example Bridger et al (76) analyzed the July 1966 heat wave in eastern Missouri and central Illinois and related the death rates of various age groups to the reported daily temperatures. Using 1965 as a "normal" period for comparison of death rates, the authors computed 3-week moving averages as shown in Figure 104-6. Of the population at risk, people 65 years old and older suffered the greatest increase in mortality, attributed chiefly to diseases of the cardiovascular system, particularly cerebrovascular disease and arteriosclerosis. Since this heat wave began suddenly and was the first truly hot spell of the year, it may have struck an essentially unacclimatized population and thus have had an especially severe effect (76).

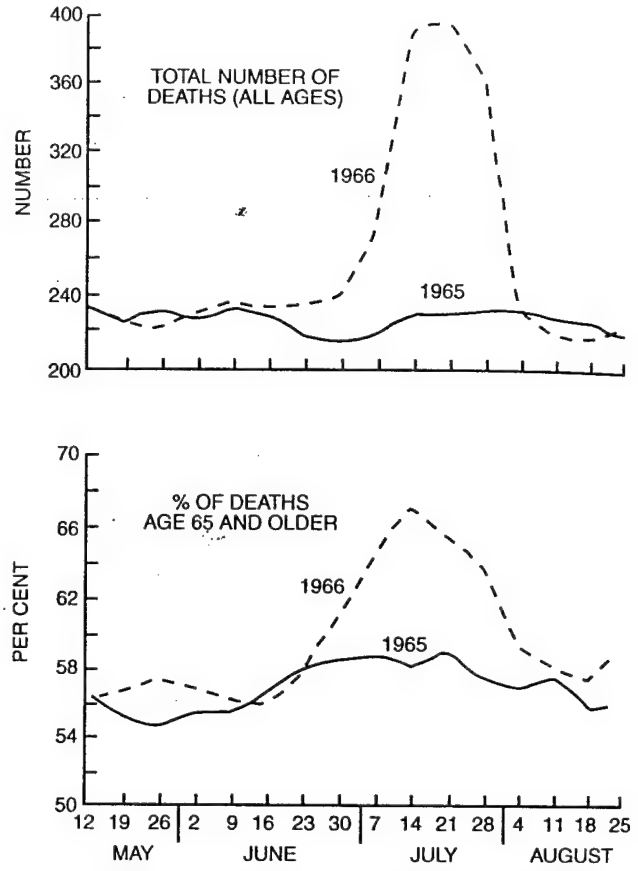

Figure 104-6 Three-week moving average of number of deaths per week in St. Louis, Mo, during the summers of 1965 and 1966 (top), and deaths occurring in those age 65 years and over expressed as a percentage of all deaths (bottom). There was a heat wave in July 1966, while the summer of 1965 was taken to represent normal weather. (Redrawn from Bridger CA, Helfand LA. Mortality from heat during July in Illinois. Int J Biometeorol 1968;12:51–70.)

Prevention

Prevention of heat illness depends on careful attention to risk factors. Candidates for occupations or other activities that subject them to prolonged or severe exercise-heat stress should be screened for individual risk factors, including use of therapeutic or recreational drugs that would increase their risk of heat illness. Unacclimatized personnel—especially those who are physically unfit—should be allowed to acclimatize gradually. Consideration should be given to excusing personnel with mild infections from activities that involve prolonged or severe exercise-heat stress. Provision should be made for adequate sleep, and alcohol abuse should be guarded against. Perhaps the most important preventive measure is ample provision of cool palatable water or other beverages, with frequent opportunity to drink. It should be stressed that although acclimatization reduces loss of salt, it does not reduce water requirements—indeed, the biophysics of heat exchange largely precludes any such effect. The persistent myth that withholding water during exercise-heat stress produces toughening is unsupported by evidence, unless rigor mortis is taken as evidence of toughness.

Persons undergoing prolonged exercise-heat stress should be encouraged to drink frequently and not to wait until they feel thirsty. Thirst is not a reliable guide to water requirements under such conditions, and complete water replacement during prolonged heat stress is difficult even if ample water is available. Soldiers on a long march, for example, gradually become progressively dehydrated if they drink only according to their feelings of thirst (77). Provision of flavored beverages may enhance consumption, but beverages should not be carbonated or caffeinated, since the former may cause a sense of fullness and the latter may promote fluid loss by diuresis. Consideration should be given to beverages containing electrolytes during intense sustained exercise-heat stress or in settings where food intake is reduced.

The views, opinions, and findings in this chapter are those of the author and should not be construed as an official Department of the Army position, policy, or decision unless so designated by other official documentation. Approved for public release, distribution is unlimited.

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13. ABSTRACT *(Maximum 200 words)*

The most important responses in humans for removing heat from the body are sweating, which increases heat loss by evaporation, and cutaneous vasodilation, which increases skin blood flow and heat transfer from core to skin. Intense exercise can increase heat production within the body ten-fold or more. For the first few minutes of exercise, most of the heat produced is retained within the body, raising core temperature until it elicits heat-dissipating responses sufficient to eliminate heat as fast as it is produced. Because of the levels of skin blood flow needed for high rates of heat dissipation in a hot environment, exercise and heat dissipation make competing demands on the cardiovascular system. In addition, if water and electrolytes lost as sweat are not replaced, plasma volume eventually is depleted, thus reducing central blood volume and impairing cardiac filling. Through these mechanisms, secondary effects of the thermoregulatory responses contribute to many of the adverse effects of heat stress, though other mechanisms related to high core temperature also have a role, especially in heat stroke. Heat tolerance is increased by aerobic exercise conditioning and by acclimatization to heat. Conversely, poor physical fitness and certain disease states and drugs are associated with impairment of the thermoregulatory responses. The foregoing factors account for most of the inter-individual differences in heat tolerance associated with gender and age.

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